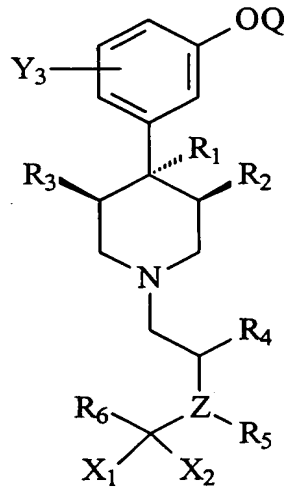
IN THE CLAIMS

Please amend the claims as follows:

--1. (Currently Amended) A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):

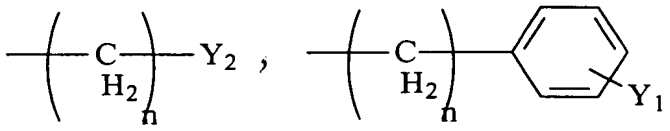
B8

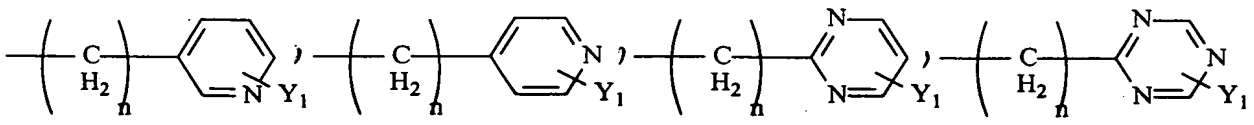


(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:





Y_1 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3, CO_2R_9, C_{1-6}alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

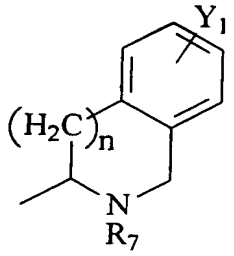
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1, CH_2aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

Z is N, O or S; where Z is O or S, there is no R_5

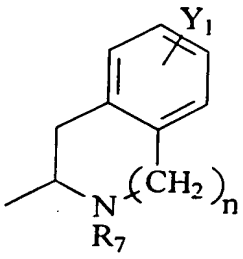
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2aryl substituted by one or more groups Y_1;

n is 0, 1, 2 or 3;

R_6 is a group selected from the group consisting of structures (a)-(bbb):



(a)



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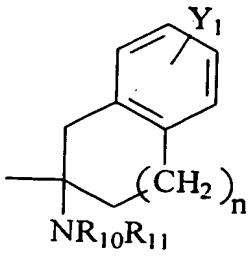

(c)

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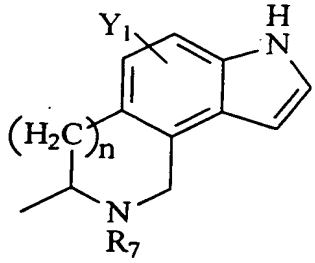

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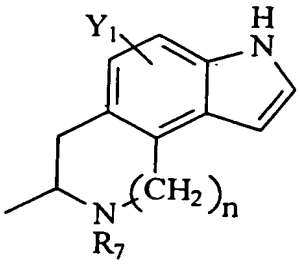

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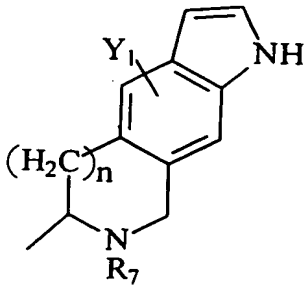

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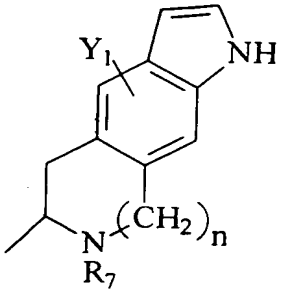

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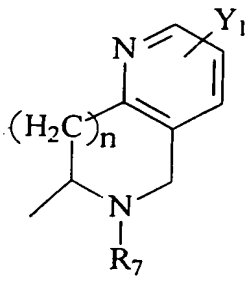

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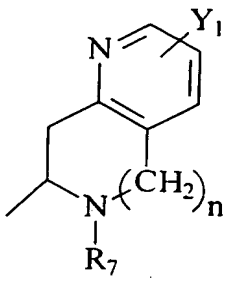

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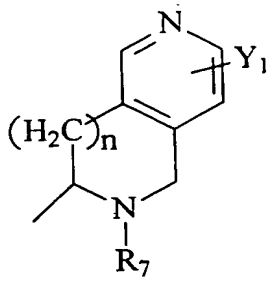

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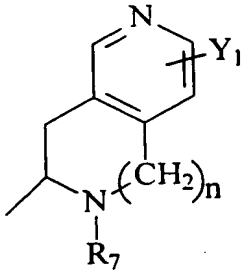

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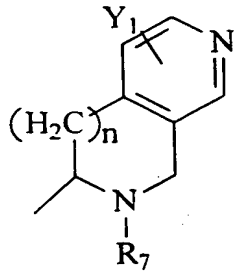

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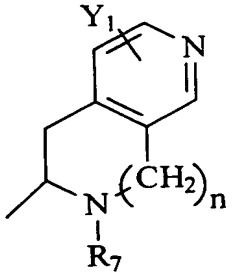

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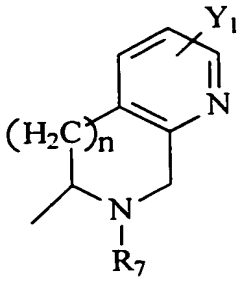

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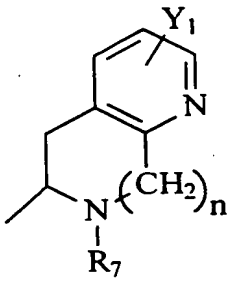

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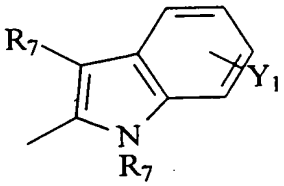

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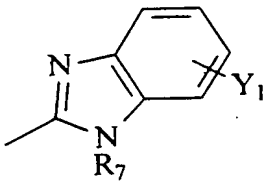

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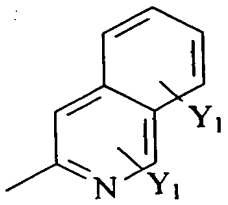

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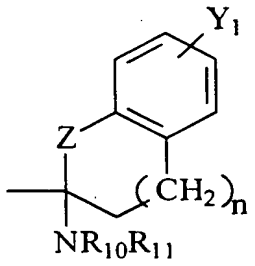

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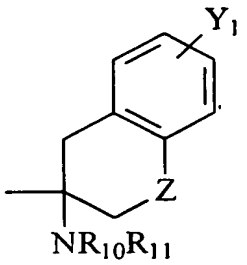

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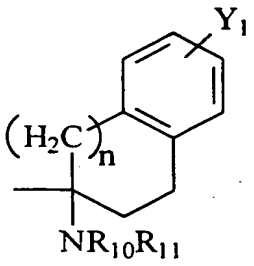

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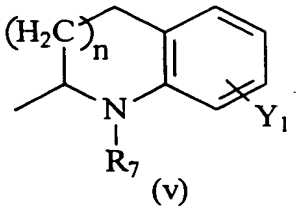

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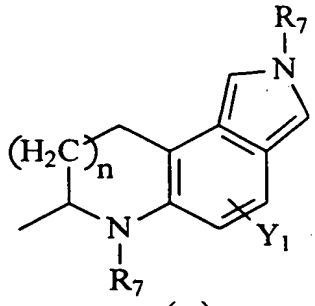

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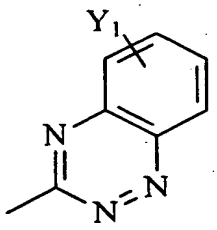

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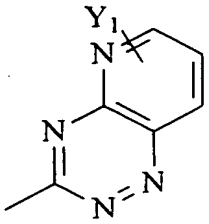

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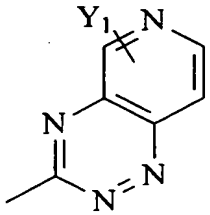

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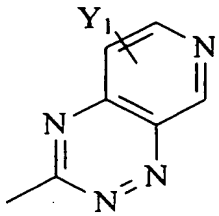

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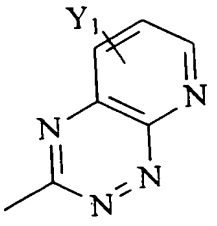

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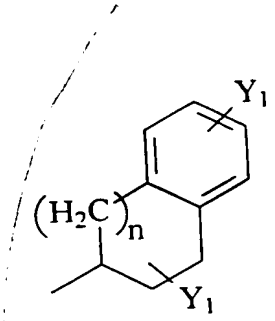

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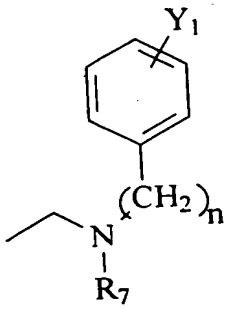

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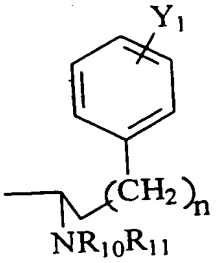

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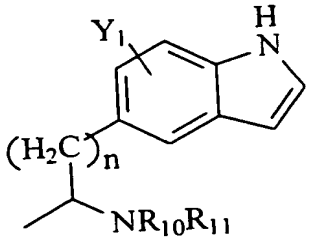

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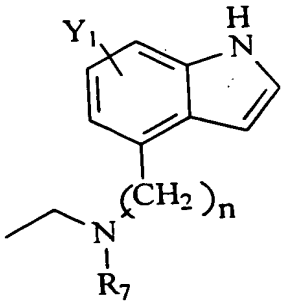

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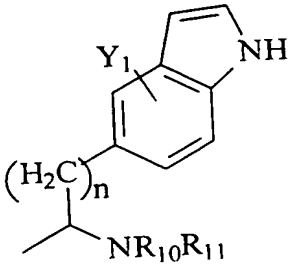

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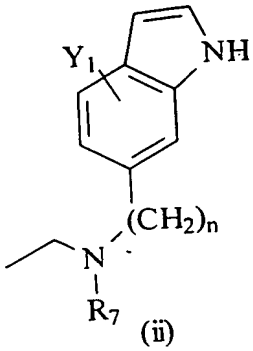

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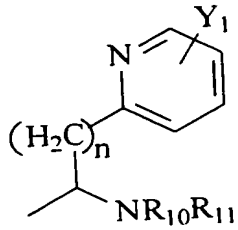

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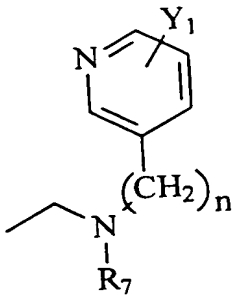

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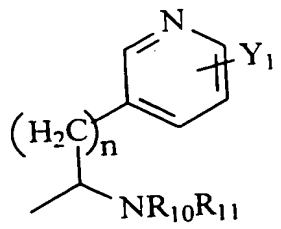

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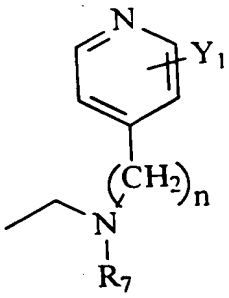

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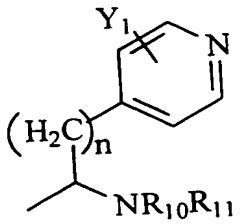

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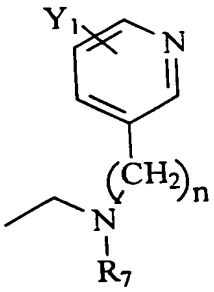

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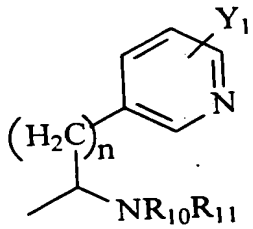

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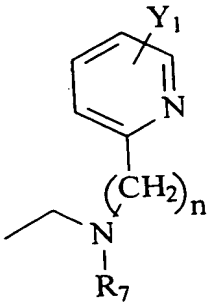

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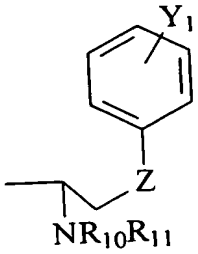

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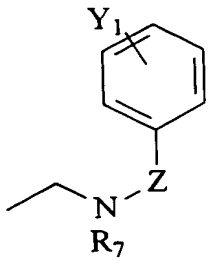

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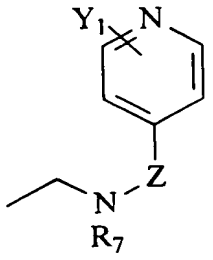

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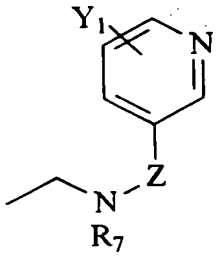

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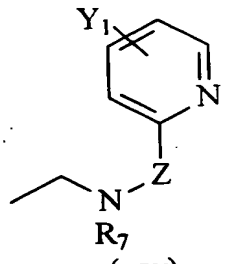

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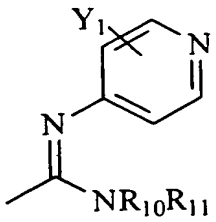

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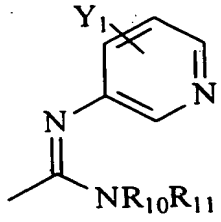

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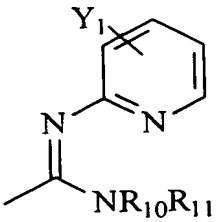

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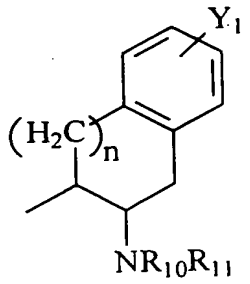

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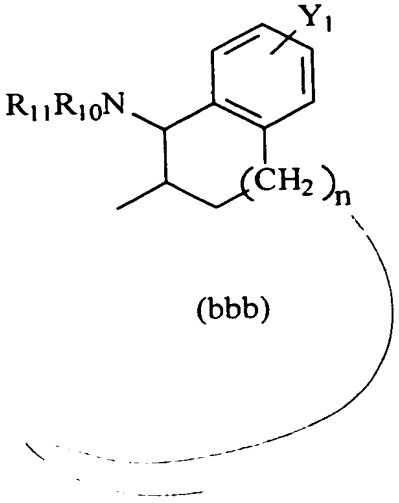

(bbb)

X_1 is hydrogen, C_{1-8} alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

X_2 is hydrogen, C_{1-8}alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

or X_1 and X_2 together form =O, =S, =NH;

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

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R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$.

2. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1, R_4, R_5, Y_1, Y_2, Z, n, X_1, X_2, and R_7-R_{17} are as ~~indicated above~~ in Claim 1;

Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2aryl substituted by one or more substituents Y_1; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(cc);

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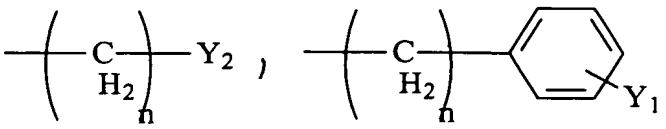
and pharmaceutically acceptable salts thereof.

3. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1, Y_2, R_4, R_5, Z, n, X_1, X_2 and R_8-R_{15} are as ~~indicated above~~ in Claim 1;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r); and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

4. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1, Z, n, X_1, X_2 and R_8-R_{15} are as ~~noted above~~ in Claim 1;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8}alkyl, ~~aryl~~ or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, or $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

5. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I),wherein Y_1, Z, n, X_1, X_2 and R_8-R_{14} are as ~~indicated above~~ in Claim 1;

R_1 is methyl,

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

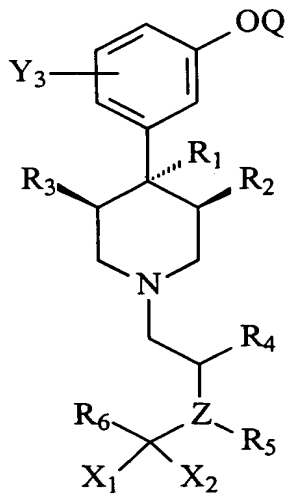
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

6. (Original) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound selected from formulae **14-21** of Fig. 1.

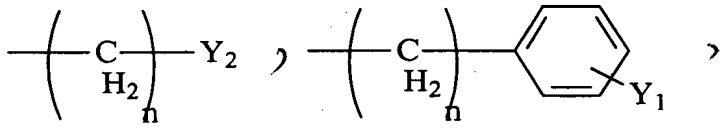
7. (Currently Amended) A kappa opioid receptor antagonist compound represented by the formula (I):

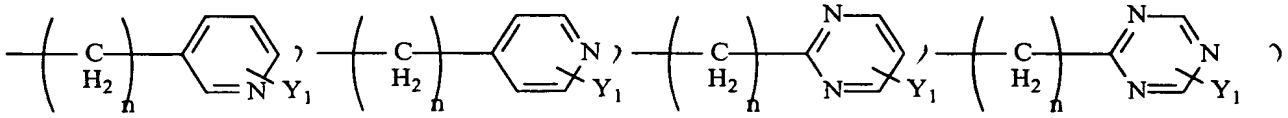


(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:





Y_1 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3, CO_2R_9, C_{1-6}alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1, CH_2aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S there is no R_5

R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2aryl substituted by one or more groups Y_1;

n is 0, 1, 2 or 3;

R_6 is a group selected from the group consisting of structures (a)-(bbb):

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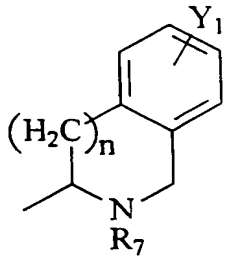
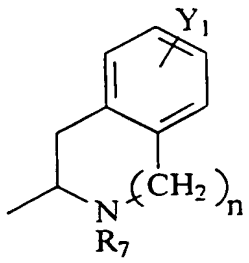
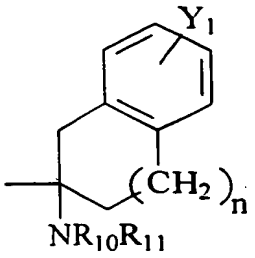


(a)



(b)



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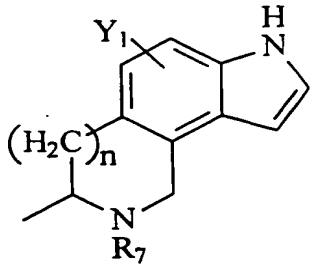

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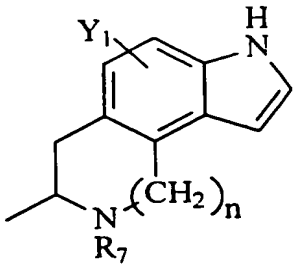

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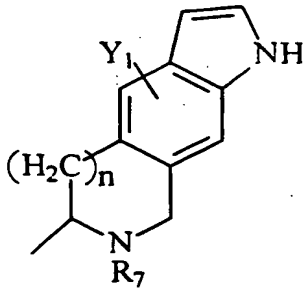

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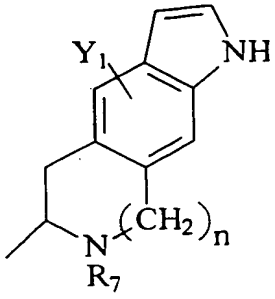

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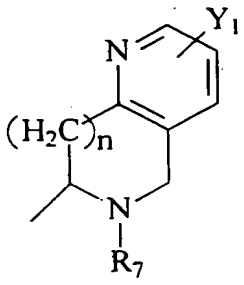

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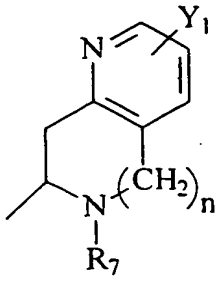
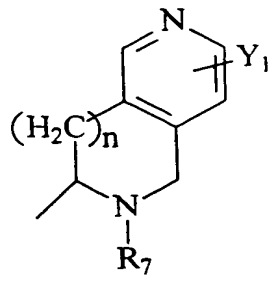


(i)



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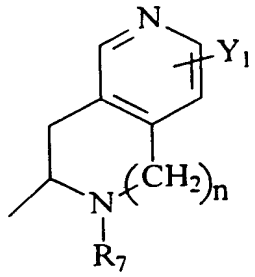

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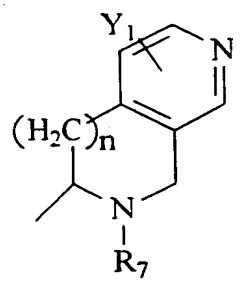

(l)

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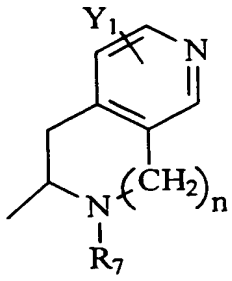

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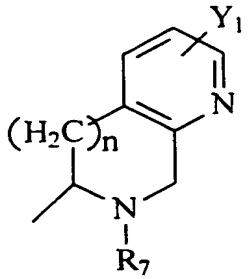

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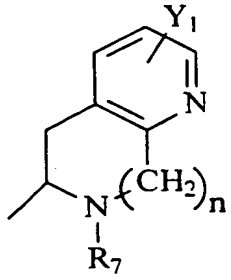

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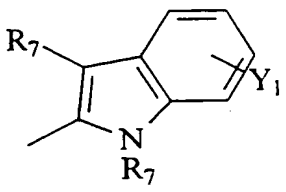

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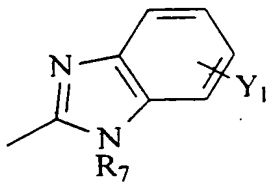

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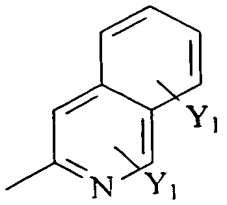

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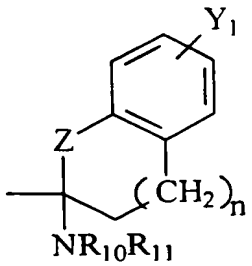

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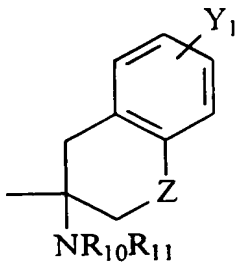

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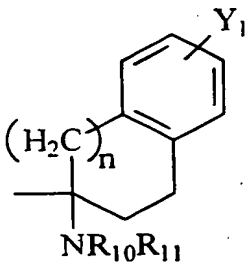

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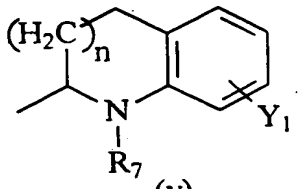
B8



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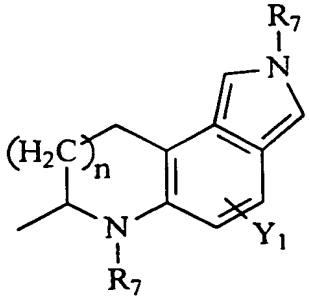

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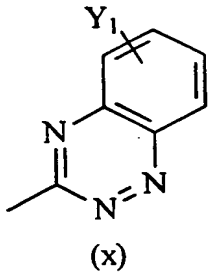

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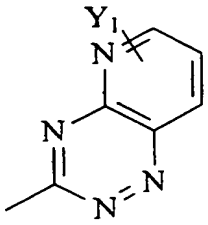

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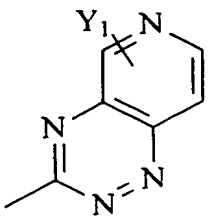

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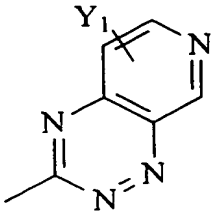

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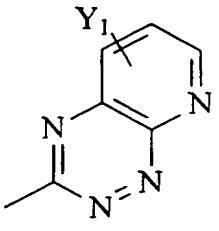

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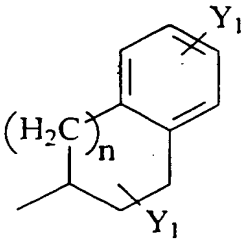

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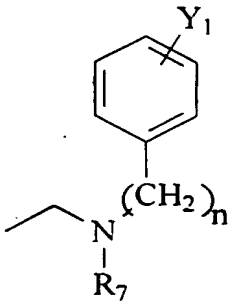

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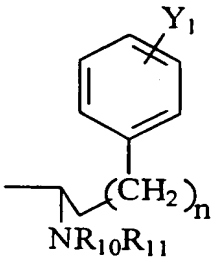

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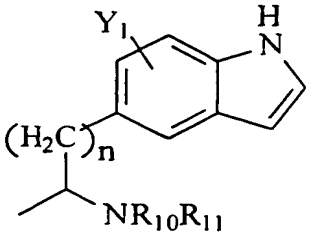
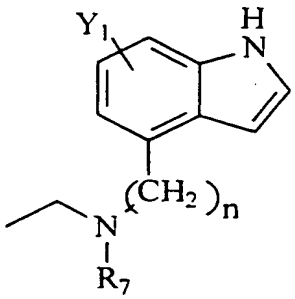


(ff)



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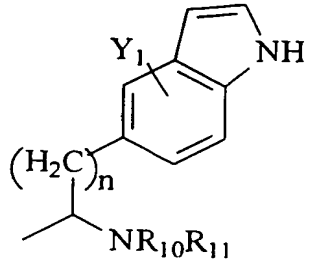

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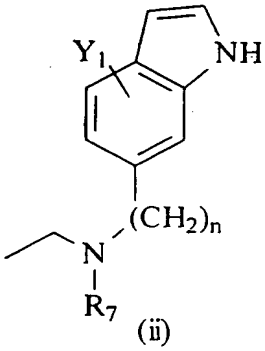

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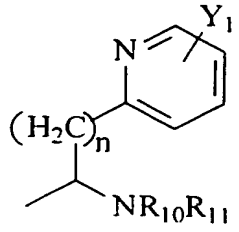

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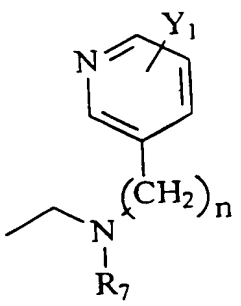
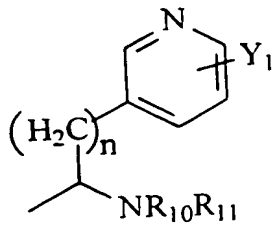


(kk)



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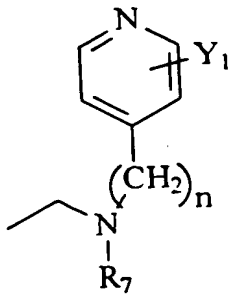

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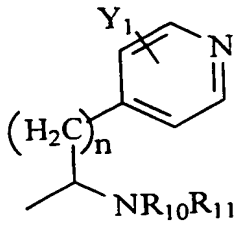

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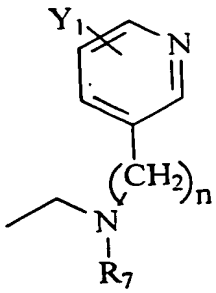

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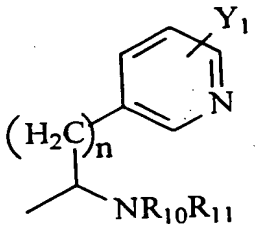

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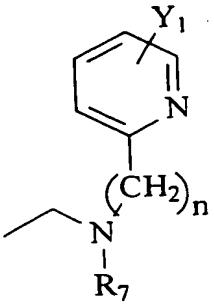

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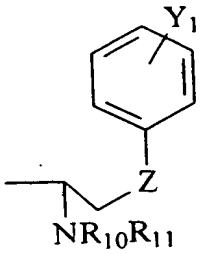

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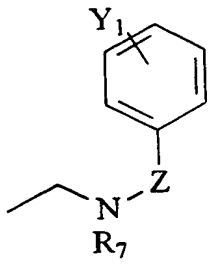

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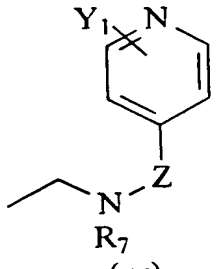

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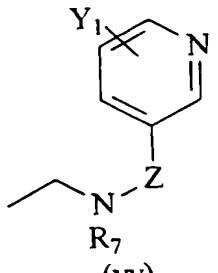

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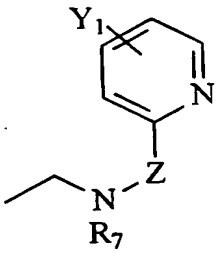

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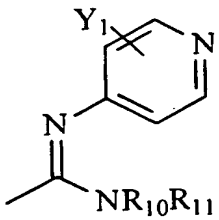

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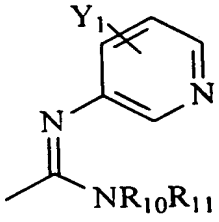

(yy)

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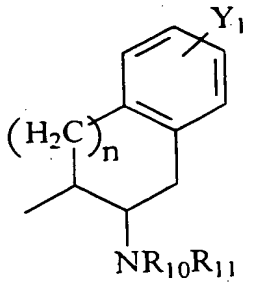

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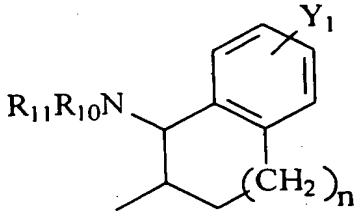

(bbb)

X_1 is hydrogen, C_{1-8} alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

X_2 is hydrogen, C_{1-8}alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

or X_1 and X_2 together form =O, =S, or =NH;

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

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R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$

and pharmaceutically acceptable salts thereof.

8. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein R_1, R_4, R_5, Y_1, Y_2, Z, n, X_1, X_2, and R_7-R_{17} are as ~~indicated above~~ in Claim 7;

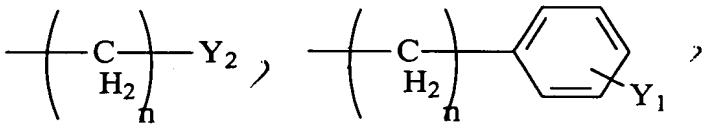
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2aryl substituted by one or more substituents Y_1; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(cc).

9. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1, Y_2, R_4, R_5, Z, n, X_1, X_2 and R_8-R_{15} are as ~~indicated above~~ in Claim 7;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r) ~~shown above~~; and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

10. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1, Z, n, X_1, X_2 and R_8-R_{15} are as ~~noted above~~ in Claim 7;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8}alkyl, ~~aryl~~ or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

11. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1, Z, n, X_1, X_2 and R_8-R_{14} are as ~~indicated above~~ in Claim 7;

R_1 is methyl,

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

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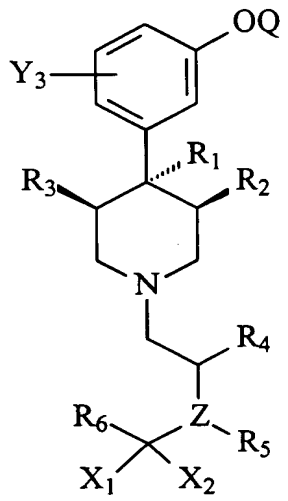
12. (Original) The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae **14-21** of Fig. 1.

13. (Currently Amended) A pharmaceutical composition comprising:

an effective amount of a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):



(I)

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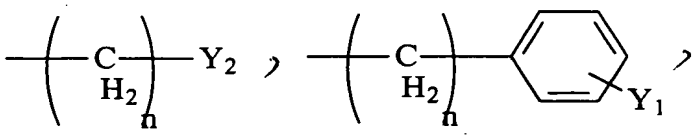
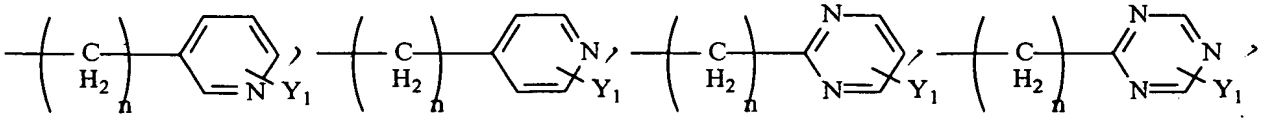
wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:





Y_1 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3, CO_2R_9, C_{1-6}alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

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R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

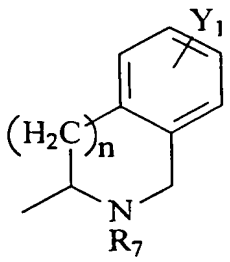
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1, CH_2aryl substituted by one or more groups Y_1, or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S, there is no R_5

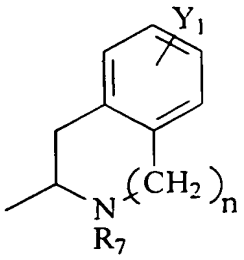
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2aryl substituted by one or more groups Y_1;

n is 0, 1, 2 or 3;

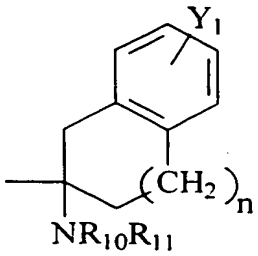
R_6 is a group selected from the group consisting of structures (a)-(bbb):



(a)



(b)



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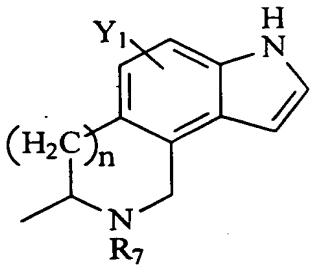

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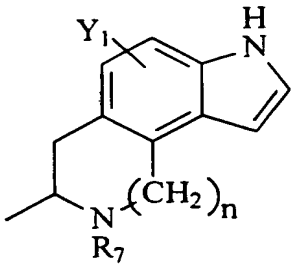
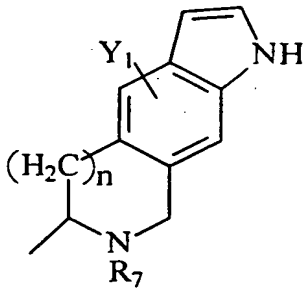


(e)



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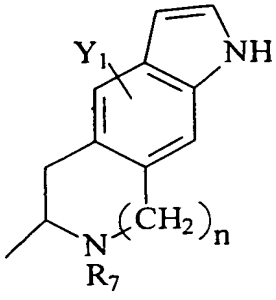
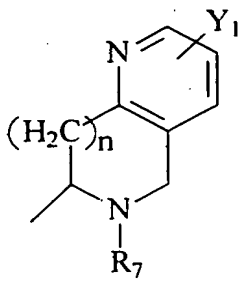
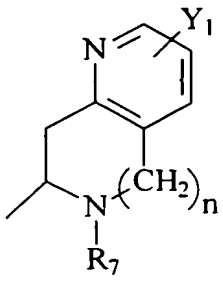


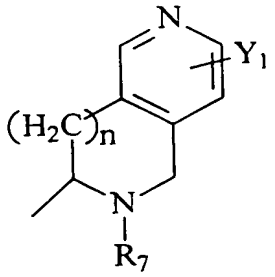
(g)



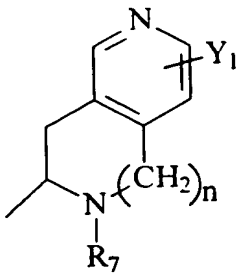
(h)



(i)



(j)



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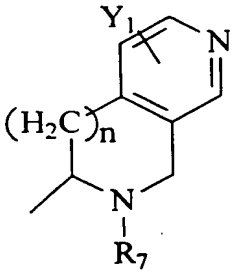

(l)

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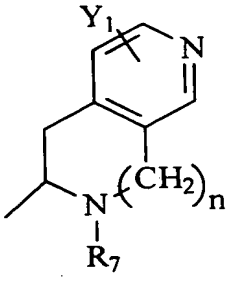
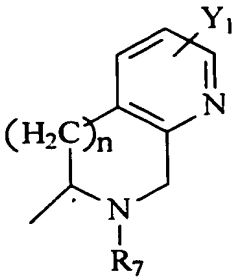
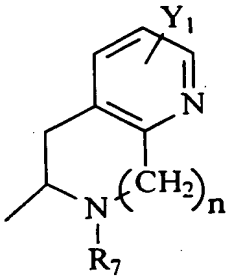


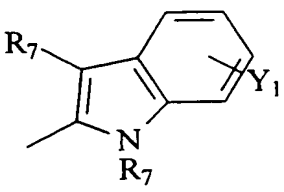
(m)



(n)



(o)



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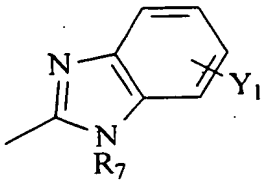

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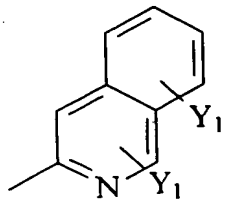

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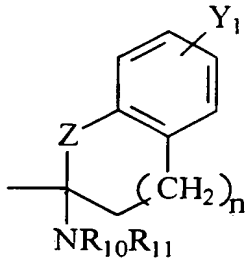

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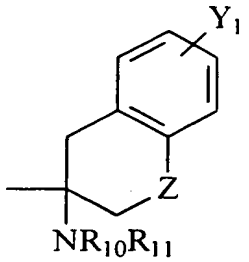

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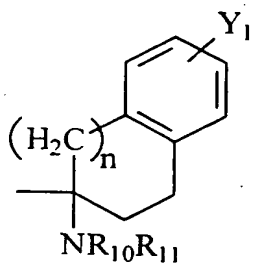

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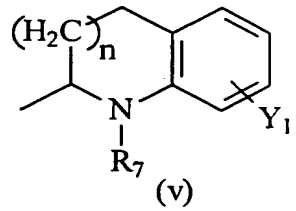

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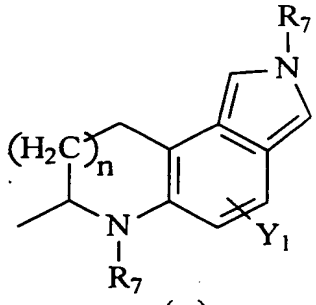

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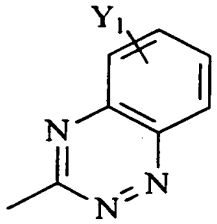

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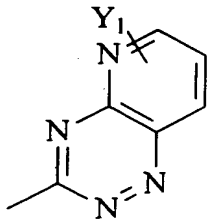

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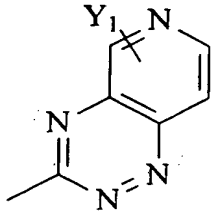

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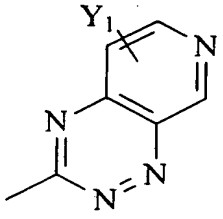

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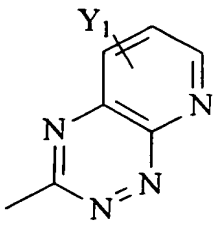

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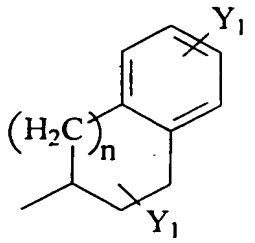

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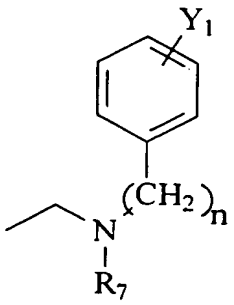

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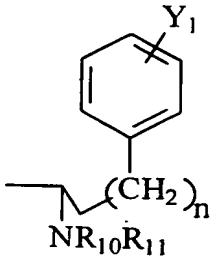

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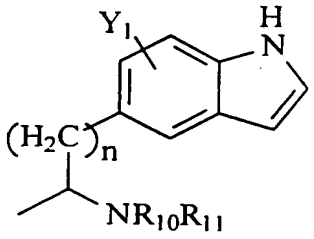

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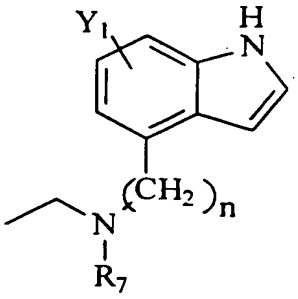

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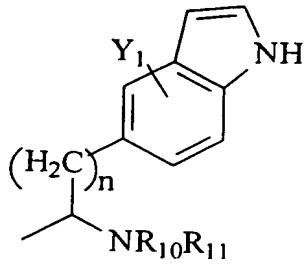

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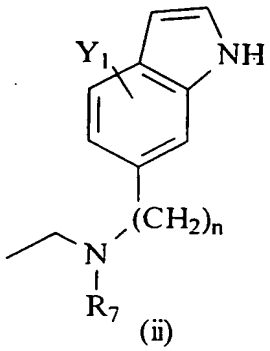

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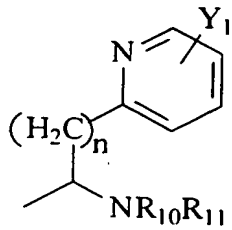

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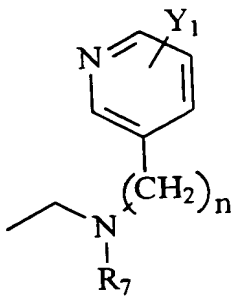

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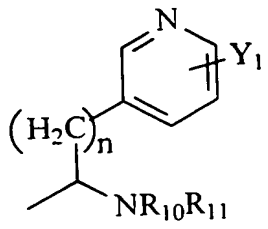

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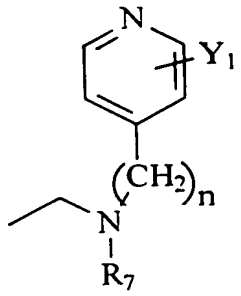

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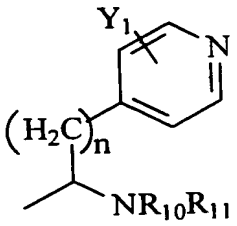

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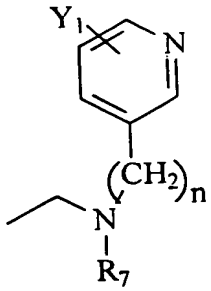

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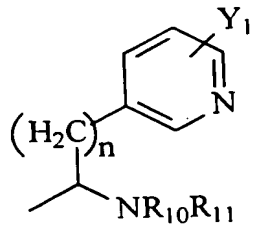

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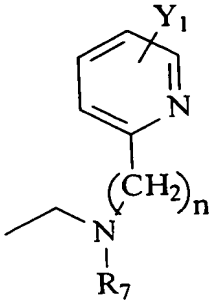

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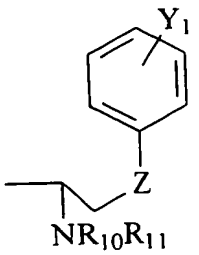

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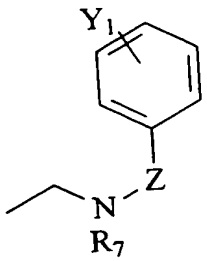

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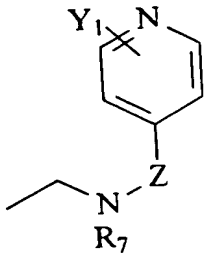

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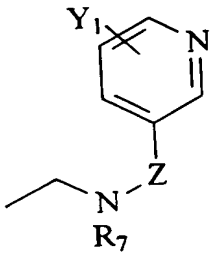

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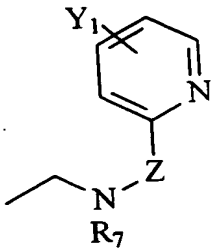

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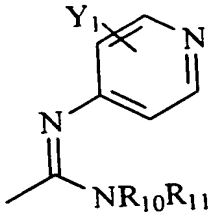

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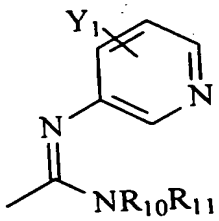

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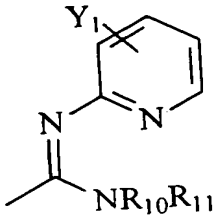

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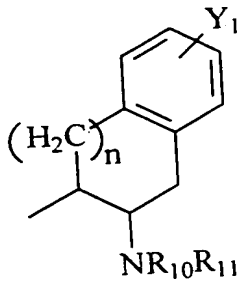

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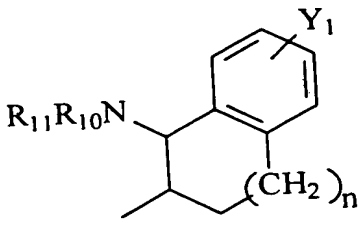

(bbb)

X_1 is hydrogen, C_{1-8} alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

X_2 is hydrogen, C_{1-8}alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

or X_1 and X_2 together form =O, =S, =NH;

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

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R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$

or a pharmaceutically acceptable salt thereof.

14. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1, R_4, R_5, Y_1, Y_2, Z, n, X_1, X_2, and R_7-R_{17} are as ~~indicated above~~ in Claim 13;

Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2aryl substituted by one or more substituents Y_1; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(cc).

15. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1, Y_2, R_4, R_5, Z, n, X_1, X_2 and R_8-R_{15} are as ~~indicated above~~ in Claim 13;

R_1 is C_{1-8} alkyl, or one of the following structures:

Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r) ~~shown above~~; and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

16. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1, Z, n, X_1, X_2 and R_8-R_{15} are as ~~noted above~~ <u>in Claim 13</u>;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, <u>or</u> $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8}alkyl, ~~aryl~~ <u>or CH_2 aryl</u> substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

17. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1, Z, n, X_1, X_2 and R_8-R_{14} are as ~~indicated above~~ in Claim 13;

R_1 is methyl,

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R_5 is H;

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R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

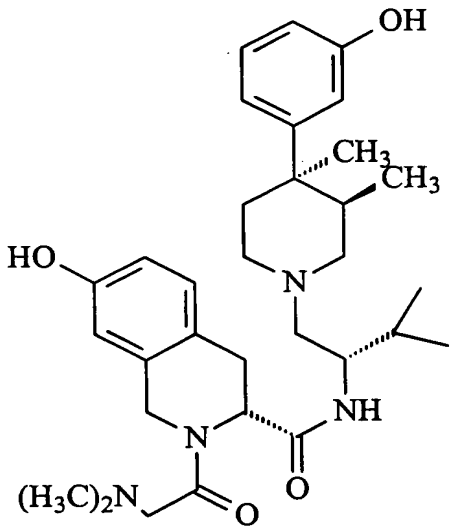
18. (Original) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae **14-21** of Fig. 1.

19. (Original) The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.

20. (Original) The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

21. (Original) The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.

22. (Currently Amended) The kappa ~~opiod~~ opioid receptor antagonist according to Claim 7, having the chemical formula:



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23. (New) The method of binding a kappa opioid receptor in a subject in need thereof, as claimed in claim 1, wherein R_1 is C_{1-8}alkyl; $(CH_2)_n$-Y_2; $(CH_2)_n$-phenyl-Y_1; or $(CH_2)_n$-pyridyl-Y_1, and R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1-Y_3, R_2-R_5, Z, n, X_1, X_2, and R_7-R_{17} are as in Claim 1.

24. (New) The kappa opioid receptor antagonist compound as claimed in claim 7, wherein R_1 is C_{1-8}alkyl; $(CH_2)_n$-Y_2; $(CH_2)_n$-phenyl-Y_1; or $(CH_2)_n$-pyridyl-Y_1, and R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1-Y_3, R_2-R_5, Z, n, X_1, X_2, and R_7-R_{17} are as in Claim 7.

25. (New) The pharmaceutical composition as claimed in claim 13, wherein R_1 is C_{1-8}alkyl; $(CH_2)_n$-Y_2; $(CH_2)_n$-phenyl-Y_1; or $(CH_2)_n$-pyridyl-Y_1, and R_6 is a group selected from

B8 the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1-Y_3, R_2-R_5, Z, n, X_1, X_2, and R_7-R_{17} are as in Claim 13.--